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Acute Myocardial Dysfunction and Recovery: A Common Occurrence After Coronary Bypass Surgery

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To evaluate whether acute myocardial dysfunction was common in the early postoperative period, serial hemodynamic measurements and radionuclide evaluation of ventricular function were performed before and after operation in 24 patients undergoing elective coronary bypass surgery. All patients had uncomplicated surgery, and no patient sustained an intraoperative infarction. In 96% of patients, significant depression in right and left ventricular ejection fraction was seen postoperatively, reaching a nadir at 262 ± 116 min after coronary bypass. Left ventricular ejection fraction was 58 ± 12% preoperatively and 37 ± 10% at trough. Right ventricular function displayed a similar pattern. These findings were also associated with depressed cardiac and left ventricular stroke work index despite maintenance of adequate ventricular filling pressures and mean arterial pressure.

The depression in ventricular function was partially reversible within 8 to 10 h after surgery. Left ventricular ejection fraction had increased to 55 ± 13% at 426 ± 77 min after coronary bypass and showed complete recovery within 48 h. Left ventricular end-systolic and end-diastolic volume index increased significantly postoperatively, but recovery in left ventricular ejection fraction was mostly due to decreases in end-systolic volume index (50 ± 22 ml at trough and 32 ± 16 ml at recovery). Depressed myocardial function was independent of bypass time, number of grafts placed, preoperative medications or core temperatures postoperatively. Postoperative therapy with pressors or inotropic agents delayed but did not prevent the occurrence of postoperative ventricular dysfunction.

Despite improvements in operative techniques and methods of myocardial protection, postoperative left ventricular dysfunction continues to be common in patients undergoing cardiopulmonary bypass surgery. Although the mechanism of myocardial depression in the early postoperative period is unclear, the results are suggestive of reperfusion injury.

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Acute myocardial dysfunction has been suggested to be a common occurrence after cardiopulmonary bypass, but its time course and frequency have not been well established (1–4). It appears to be a reversible event within 24 h of surgery and may have profound importance in the early postoperative period, especially in patients with already compromised ventricular function. This may have an effect on patient management and on the assessment of early postoperative morbidity and mortality. Although its origin remains unclear, some studies (5,6) have suggested that inadequate myocardial protection or the effects of cold cardioplegia may play a role. Recent studies (7–9) have implicated reperfusion injury secondary to oxygen-derived free radicals after cardiopulmonary bypass.

To further evaluate this process, serial hemodynamic and radionuclide monitoring was utilized to assess right and left ventricular function in the pre- and postoperative period in 24 patients undergoing elective uncomplicated coronary bypass surgery. This approach was used to determine how frequently biventricular dysfunction occurred, assess its reversibility and define the role of routine postoperative therapy.

Methods

Study patients. Twenty-four patients undergoing routine elective coronary bypass surgery completed the study. Pa-

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Table 1. Clinical Data in 24 Patients

Mean age (yr)	63 ± 11
No. of grafts	3.2 ± 0.9
Ischemic time (min)	57 ± 18
CPB time (min)	105 ± 26
Preop medications (no. of patients)	
Nitrates	13 (1, 2, 5, 8–10, 12–14, 18, 20, 22, 23)
Beta-blockers	15 (1, 3, 5, 6, 8–12, 14, 18–21, 24)
Ca antagonists	19 (1, 3–5, 7–9, 11–20, 22, 23)
Core temperature (°C)	
Immediately postop	36 ± 0.7
Trough	36.7 ± 1.0
Recovery	37.2 ± 0.8
Therapy received within 8 h of CPB (no. of patients)	
None	7 (6, 7, 9, 16, 21, 22, 24)
Dobutamine	11 (1–3, 5, 11–14, 17, 18, 20)
Dopamine	9 (4, 5, 8, 10, 12, 14, 15, 18, 20)
Nipride	9 (1, 3, 5, 11, 13, 14, 18, 19, 23)
Nitroglycerin	4 (13, 17, 20, 23)
Neosynephrine	2 (2, 18)

Ca = calcium channel; CPB = cardiopulmonary bypass; postop = postoperatively; Preop = preoperative; numbers in parentheses indicate patient number; numbers to the right of ± signs indicate standard deviation.

tients undergoing repeat coronary surgery as well as those with unstable angina or concurrent valve repair or aneurysm resection were excluded. Five patients who initially signed informed consent were excluded; one had an extensive intraoperative myocardial infarction, three had a poor radionuclide tag and one had inadequate positioning with the nuclear probe. There were 19 men and 5 women, with a mean age of 63 ± 11 years. Preoperative medical therapy is indicated in Table 1; all patients were on antianginal therapy. The mean number of grafts placed was 3.2 ± 0.9, with a 57 ± 18 min ischemic time and a 105 ± 26 min cardiopulmonary bypass time. All patients enrolled in the study gave informed consent. The study was approved by the Institutional Review Board of Biomedical Research and Radiation Safety Committee.

Pre- and intraoperative evaluation. All patients had radionuclide angiography and nuclear probe studies performed preoperatively to determine baseline ejection fraction and regional wall motion and to correlate the gamma camera and nuclear probe findings. The best left anterior oblique view for evaluating the left ventricular region of interest was also assessed. Labeling was performed with 25 mCi of technetium pertechnetate by the modified in vivo labeling technique (10). Three view-gated blood pool studies were performed with a mobile GE Starcam. Ejection fraction was calculated in the "best septal" left anterior oblique view as a 32 frame study, with 250,000 counts obtained per frame. The ventricular region of interest was identified with a semiautomated edge detection program that used both second derivative and threshold techniques. Ejection fraction determination also relied on the use of periventricular background subtraction and a variable region of interest. Nuclear probe studies were performed with the NIC II (Bios), which is a high temporal resolution (10 ms) nonimaging device (11–13). All studies were performed for 60 s, and background activity was determined in both a manual and automatic mode. All probe studies were performed by one operator who had great proficiency with this device.

Before surgery, a right ventricular ejection fraction catheter was placed in the pulmonary artery. This fast response thermodilution catheter (REF 1-Baxter Edwards) uses an onboard computer to exponentially fit the thermodilution output curve so that right ventricular volumes and right ventricular ejection fraction can be determined (14,15). Thermodilution right ventricular ejection fraction with this technique correlates well with contrast and radionuclide ventriculography over a wide range of ejection fractions, however, in patients with significant tricuspid regurgitation, a wide range of error can be seen (16). Other hemodynamic measurements recorded included heart rate, right atrial pressure, pulmonary artery pressure, pulmonary capillary wedge pressure and mean systemic arterial pressure. Cardiac output and right ventricular ejection fraction were determined with iced dextrose in water in triplicate at 15 min intervals pre- and intraoperatively by an experienced user of this catheter. The three measurements were averaged if they were within 10% of each other; curves judged to be "bad" by the computer were excluded.

Postoperative evaluation. Within 131 ± 13 min after cardiopulmonary bypass, patients arrived in the surgical intensive care unit and were again labeled with 25 mCi of technetium pertechnetate. The nuclear probe was positioned over the left ventricular region of interest, and serial determinations of left ventricular ejection fraction and filling variables were recorded. Nuclear probe and hemodynamic measurements were obtained serially at 15 min intervals for up to 10 h (mean 8.8 ± 0.8) after operation. An automated background approach was utilized with the nuclear probe (78% of end-diastolic counts), but background was rechecked manually and recorded at hourly intervals during the study. Repeat radionuclide angiograms were performed within 4 h of surgery and at 24 to 48 h postoperatively. Serial hemodynamic assessment included systolic and diastolic blood pressure, as well as all preoperative measurements recorded together with right ventricular ejection fraction and cardiac output. Other variables recorded included core temperatures, arterial oxygen saturation and concordant medical therapy (including pressors and vasodilators (Table 1). Left ventricular volumes, and stroke work index and systemic vascular resistance were calculated from the recorded measurements. No patient required intraaortic balloon counterpulsation to come off cardiopulmonary bypass. All pa-

tients had serial electrocardiograms and cardiac enzymes determined for 48 h postoperatively.

Statistics. All data are displayed as mean values ± SD. Each patient served as his or her own control from preoperative to postoperative measurements. Comparisons between pre- and postoperative variables were evaluated with a *t* test. Analysis of variance for repeated measures was used to test differences between serial measurements for a given variable postoperatively. If differences were found, a paired Student's *t* test was used to determine significance at $p < 0.05$. Radionuclide angiograms were read by an independent observer with no knowledge of the patients' hemodynamic or nuclear probe results.

Results

Cardiac bypass surgery was uncomplicated in the 24 patients studied, with no patient having a intraoperative myocardial infarction based on standard criteria (17). Intermittent blood cardioplegia was used for all patients intraoperatively and did not change during the course of the study. Therapy received postoperatively, number of grafts, ischemic time and core temperatures are indicated (Table 1). Sixty-three percent of patients were placed on dopamine or dobutamine within 8 h of cardiopulmonary bypass; only 29% required no therapy with vasopressors, inotropic agents or vasodilators. All therapeutic decisions concerning postoperative patient management were made by the cardiothoracic or critical care fellows, independent of the ejection fraction data recorded.

Depression and recovery of biventricular function (ejection fraction response). Left ventricular ejection fraction was depressed in the immediate postoperative period in 19 (79%) of the 24 patients approximately 2 h after cardiopulmonary bypass. In 4 additional patients, the decrease in left ventricular ejection fraction was delayed, and in 23 of 24 patients, it continued to worsen, reaching a nadir (trough level) at 262 ± 116 min after cardiopulmonary bypass (Fig. 1, Table 2). The decline in left ventricular ejection fraction was highly significant, with a preoperative mean value of 58 ± 12%, decreasing to 46 ± 12% immediately postoperatively and 37 ± 10% at trough. One patient (Patient 4) had an increase in left ventricular ejection fraction in the immediate postoperative setting and despite a subsequent decline, it never decreased to below preoperative levels. Significant recovery of left ventricular ejection fraction to 55 ± 13% occurred in all patients during the 8 to 10 h study (426 ± 77 min after cardiopulmonary bypass). Full recovery of left ventricular function was seen in all patients at the time of the 24 to 48 h gated blood pool study. Correlation of nuclear probe and radionuclide angiographic studies was very good ($r = 0.92$, SEE ± 5) for pre- and postoperative studies over a wide range of ejection fraction.

Right ventricular ejection fraction was somewhat lower than left ventricular ejection fraction before operation (52 ± 9%), but postoperative changes in right ventricular ejection fraction paralleled those in the left ventricle (Table 2). In the initial postoperative period, right ventricular ejection fraction was mildly depressed (45 ± 11%), but at the time of maximal left ventricular depression, it had decreased to 36 ± 14%. In 12 patients, left and right ventricular trough values occurred at the same time, and in 9 additional patients, they were within 30 min of each other. Recovery of right ventric-

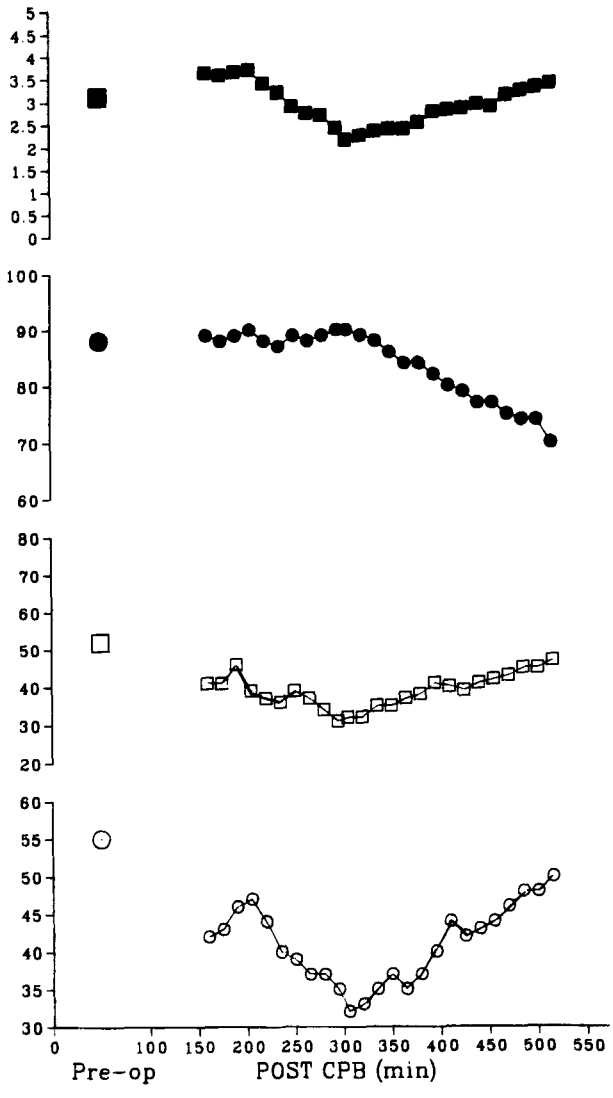

Figure 1. Patient 3. Hemodynamic biventricular ejection fraction responses. Shown from **top to bottom** are cardiac index (CI), mean arterial pressure (MAP), right ventricular ejection fraction (RVEF) and left ventricular ejection fraction (LVEF). This patient was treated with dobutamine and nitroprusside shortly after surgery and initially had a well preserved cardiac index. Right and left ventricular ejection fraction were depressed in the early postoperative period, but continued to worsen, reaching a nadir at 304 min after cardiopulmonary bypass (CPB). This was associated with a significant decrease in cardiac index. Significant recovery in all postoperative variables was seen at 515 min after cardiopulmonary bypass.

Table 2. Pre- and Postoperative Ventricular Function in 24 Patients Undergoing Uncomplicated Coronary Bypass Surgery

	Preop			Immed Postop				Trough				Recovery			
Pt. No.	LVEF	RVEF	CI	LVEF	RVEF	CI	Time Post CPB	LVEF	RVEF	CI	Time Post CPB to LV Trough	LVEF	RVEF	CI	Time Post CPB to LV Recovery
1	66	72	2.62	54	53	6.05	135	48	29	4.00	288	60	35	5.05	423
2	45	53	3.43	34	34	2.55	145	26	23	1.86	233	33	50	3.75	383
3	55	52	3.12	42	41	3.63	160	32	32	2.16	305	46	47	3.41	515
4	43	51	2.85	56	50	4.38	130	43	33	3.80	398	50	48	4.86	518
5	64	56	2.51	56	62	2.34	142	38	61	1.70	282	52	55	1.69	312
6	42	48	1.64	34	25	1.72	139	33	24	1.70	154	46	41	2.10	469
7	66	49	3.45	34	34	1.75	123	34	34	1.76	123	58	44	3.25	378
8	49	49	2.82	49	38	3.34	145	37	41	3.29	285	55	43	3.23	450
9	70	64	2.04	48	60	2.43	130	48	60	2.43	150	54	52	3.10	451
10	57	66	3.72	55	57	3.69	150	24	49	3.07	438	44	50	4.49	543
11	73	51	2.81	51	55	2.58	130	39	43	2.34	249	66	54	3.80	474
12	61	40	—	74	37	2.81	135	32	20	1.35	350	53	33	2.56	410
13	52	56	2.54	30	46	1.98	105	26	34	2.99	150	44	47	2.93	420
14	48	55	3.13	23	52	2.46	120	19	58	2.04	147	39	58	3.40	477
15	57	42	2.16	54	60	4.36	120	31	42	3.08	465	63	62	6.00	495
16	84	61	2.47	53	26	2.06	140	46	13	1.88	480	76	33	4.16	510
17	51	52	2.56	44	43	2.29	120	39	36	1.84	225	53	42	3.36	375
18	40	54	2.87	32	40	3.67	123	17	5	1.64	408	34	17	2.96	468
19	42	43	2.51	34	39	2.31	120	34	39	2.31	120	48	32	2.95	225
20	57	55	3.26	48	50	2.25	121	42	33	2.08	324	55	51	2.71	444
21	60	29	2.65	44	39	2.21	125	44	39	2.21	125	81	52	3.91	365
22	80	57	3.07	44	47	2.06	115	44	47	2.06	115	80	51	3.39	400
23	69	47	3.27	63	62	3.89	127	47	46	3.42	212	58	49	3.77	437
24	67	51	2.59	53	39	2.69	140	55	33	2.71	260	77	44	3.35	290
Mean	58	52	2.8	46	45	2.9	131	37	36	2.4	262	55	45	3.5	426
±SD	12	9	0.6	12	11	1.0	13.0	10	14	0.7	116	13	10	0.9	77

CI = cardiac index (liters/min per m^2); CPB = cardiopulmonary bypass (min); Immed = immediately; LV = left ventricular; LVEF = left ventricular ejection fraction (%); Post = after; Postop = postoperatively; Preop = preoperatively; Pt. = patient; RVEF = right ventricular ejection fraction (%).

ular function displayed a similar pattern as that of the left ventricle and was almost complete in patients at 8 to 10 h after cardiopulmonary bypass (45 ± 10% at recovery) and showed full recovery by 24 h as judged by radionuclide angiography. Depression and recovery of right and left ventricular function were independent of patients' core temperature or hemodynamic profile but were somewhat related to therapy received.

Hemodynamic changes after cardiopulmonary bypass. Preoperative mean arterial pressure (86 ± 10 mm Hg) and ventricular filling pressures (pulmonary capillary wedge pressure [13 ± 3 mm Hg] and central venous pressure [7 ± 2 mm Hg]) were maintained in patients postoperatively when possible, with fluids or supportive medications (Table 3). Heart rate increased from a 66 ± 11 beats/min preoperatively to 96 ± 20 beats/min postoperatively and remained relatively constant during the postoperative portion of the study. Cardiac index, although initially stable in the postoperative period (2.9 ± 1.0 liters/min per m^2), decreased significantly at the nadir of left ventricular function (2.4 ± 0.7 liters/min per m^2), but increased beyond preoperative levels (3.5 ± 0.9 liters/min per m^2) at recovery (Table 2). This increase beyond baseline values may be a reflection of the number of patients placed on inotropic or vasodilator therapy. Changes in left ventricular volumes suggested that significant systolic left ventricular dysfunction occurred in the postoperative period (left ventricular end-systolic volume index increased from 39 ± 21 ml immediately after operation to 50 ± 22 ml at the nadir in the left ventricular ejection fraction). At recovery, there was a significant decrease in left ventricular end-systolic volume index to 32 ± 16 ml ($p = 0.003$). Changes in left ventricular end-diastolic volume index were also significant from immediate postoperative to trough levels, but the major improvement in left ventricular ejection fraction at recovery reflected significant decreases in end-systolic volume index. Left ventricular stroke work index was depressed postoperatively (33 ± 11 g-m/m^2) and continued to worsen at trough levels of ventricular function (29 ± 13 g-m/m^2). At recovery, there was an improvement in left ventricular stroke work index (37 ± 9 g-m/m^2, $p = 0.02$), although it still remained below normal preoperative levels. Systemic vascular resistance index was unchanged initially

Table 3. Postoperative Hemodynamic Assessment of Left Ventricular Function in 24 Patients

Pt. No.	Immed Postop						Trough						Recovery					
	LVEDVI	LVESVI	LVSWI	HR	MAP	PCWP	LVEDVI	LVESVI	LVSWI	HR	MAP	PCWP	LVEDVI	LVESVI	LVSWI	HR	MAP	PCWP
1	122	56	58	91	77	16	92	48	67	90	118	14	78	31	58	108	100	15
2	79	52	27	96	79	10	81	60	18	90	74	10	103	69	38	110	85	14
3	81	47	38	108	89	11	88	60	30	77	90	14	98	53	36	80	70	10
4	84	37	52	94	90	11	86	49	37	104	84	12	88	44	44	110	79	10
5	61	27	27	69	72	15	63	39	22	71	78	12	44	21	25	72	84	13
6	68	45	27	76	94	12	67	45	25	76	91	12	57	31	24	80	75	12
7	82	54	26	62	72	10	82	54	26	62	72	10	67	28	37	84	78	11
8	76	39	31	91	72	13	100	63	33	88	72	12	62	28	29	96	73	11
9	63	33	30	80	74	6	63	33	30	80	74	6	63	29	34	90	81	12
10	60	27	35	112	82	9	100	76	21	126	70	12	82	46	31	124	71	11
11	43	21	28	116	94	10	51	31	25	116	100	9	62	21	45	92	87	13
12	32	8	20	118	67	8	50	34	17	87	89	13	51	24	30	96	93	13
13	80	56	33	82	102	10	112	83	43	104	117	13	66	37	41	100	108	10
14	135	104	43	80	112	10	137	111	37	80	106	8	105	64	48	82	86	7
15	70	32	33	116	69	9	94	65	18	106	56	12	76	28	44	126	77	14
16	38	18	22	104	86	8	43	23	16	94	68	11	49	12	45	112	95	10
17	39	22	15	132	73	10	46	28	15	104	73	12	53	25	31	118	94	16
18	91	62	26	125	77	15	88	73	14	108	83	18	75	49	24	118	80	12
19	103	68	56	66	121	10	103	68	56	66	121	10	75	39	30	82	68	10
20	56	29	31	82	90	11	62	36	25	80	80	13	64	29	35	77	82	12
21	43	24	28	116	115	14	43	24	27	116	115	14	48	9	31	101	72	16
22	61	34	30	76	88	10	61	34	30	76	88	10	46	9	44	92	95	11
23	51	19	45	122	106	8	66	35	38	109	94	8	57	24	30	115	74	8
24	57	27	40	89	107	15	56	25	33	88	83	10	52	12	48	84	98	14
Mean	70	39	33	96	88	11	76	50	29	92	87	12	68	32	37	98	84	12
±SD	26	21	11	20	16	3	24	22	13	17	18	3	18	16	9	16	11	3

HR = heart rate (beats/min); LVEDVI = left ventricular end-diastolic volume index (ml/m^2); LVESVI = left ventricular end-systolic volume index (ml/m^2); LVSWI = left ventricular stroke work index (g-m/m^2); MAP = mean arterial pressure (mm Hg); PCWP = pulmonary capillary wedge pressure (mm Hg); other abbreviations as in Table 2.

Table 4. Role of Concordant Therapy in the Timing of Ventricular Dysfunction Postoperatively

	Group 1 (n = 9) No Pressors Required					Group 2 (n = 15) Pressor or Inotropic Therapy				
	LVEF	p Value	RVEF	p Value	Time Post CPB	LVEF	p Value	RVEF	p Value	Time Post CPB
Preop	64 ± 15		50 ± 10			55 ± 9		54 ± 8		
		0.006		0.08			NS		0.06	
Postop	45 ± 10		41 ± 13		129 ± 11	47 ± 13		48 ± 9		132 ± 14
		NS		NS			0.002		0.009	
Trough	43 ± 8		37 ± 14		193 ± 18	33 ± 9		36 ± 14		303 ± 96
		0.001		NS			0.001		0.03	
Recovery	64 ± 14		44 ± 8		392 ± 90	50 ± 10		46 ± 11		447 ± 62

$p < 0.05$ (significant) reflects differences between the two associated measurements. Abbreviations as in Table 2.

after operation (2,320 ± 380 preoperatively versus 2,443 ± 948 dyne·s·cm^{-5}·m^2 postoperatively), but at maximal left ventricular depression, it increased to 2,780 ± 902 dyne·s·cm^{-5}·m^2. At recovery, there was a highly significant improvement in systemic vascular resistance index to 1,808 ± 568 dyne·s·cm^{-5}·m^2, which may reflect therapy received and the normal vasodilatory response seen after surgery.

Radionuclide angiography. Postoperative radionuclide angiograms were performed in both a left anterior oblique and anterior view within 4 h of cardiopulmonary bypass in 20 patients and at 24 to 48 h in all patients. Postoperative studies correlated with the nuclear probe studies and were helpful in evaluating changes in left and right ventricular function. No patient developed a new regional wall motion abnormality in the postoperative period. In nine patients, the initial postoperative radionuclide angiogram was performed when there was no significant difference between the preoperative and postoperative nuclear probe ejection fraction and the only new finding was paradoxic septal motion. In 11 patients, the postoperative study demonstrated diffuse left ventricular hypokinesia, paradoxic septal motion and, in 6 patients, left ventricular dilation. In 11 patients, right ventricular function was assessed as normal on the radionuclide study, but in 9 patients, right ventricular dilation and marked hypokinesia were also present. The 24 to 48 h study in all patients showed full recovery of left ventricular function, and in six patients, there was improvement beyond preoperative ejection fraction levels. Right ventricular function was assessed as normal in all patients at the 24 to 48 h study.

Timing of left ventricular dysfunction and the role of concurrent therapy. Of the 24 patients, 7 received no postoperative medication and 2 received only intravenous nitroglycerin or nitroprusside (Group 1). The remaining 15 patients required pressor or inotropic therapy (Group 2) during the initial postoperative period, but both groups had normal baseline left ventricular function (Table 4). Patients in Group 1 had a higher preoperative ejection fraction than did patients in Group 2 (Group 1 64 ± 15% versus Group 2 55 ± 9%, $p = 0.08$), but no patient in either group had a baseline left ventricular ejection fraction <40%, and only one patient in Group 1 and six patients in Group 2 had an ejection fraction <50%. Patients in Group 1 reached trough ejection fraction levels significantly earlier in the postoperative period (Group 1 193 ± 18 min versus Group 2 303 ± 96 min, $p = 0.02$). Both groups manifested similar degrees of left ventricular dysfunction during the study (33% versus 40% decrease in ejection fraction in Group 1 and Group 2, respectively), but early postoperative ventricular dysfunction was less marked in Group 2 patients receiving pressor or inotropic therapy. Its occurrence, however, could not be prevented by therapy, only delayed. Significant recovery toward baseline occurred in both groups over the same time period despite different therapies received (Group 1 392 ± 90 min versus Group 2 447 ± 62 min, p = NS). Depression and recovery of right ventricular function displayed a similar pattern in both groups. There were no differences between groups with respect to patient characteristics, preoperative therapy, core temperature, number of coronary grafts or aortic cross-clamp time.

Discussion

Despite improvements in surgical technique, methods of cardioplegia and intraoperative anesthesia and monitoring, acute myocardial dysfunction continues to be a common problem early after elective coronary bypass surgery, as seen in 96% of patients who were serially evaluated before and after operation in this study. Although myocardial dysfunction was reversible within 8 to 10 h of surgery, with complete recovery of ventricular function by 48 h, its occurrence in the majority of patients raises concerns.

Previous studies. Previous studies by Roberts et al. (1,2) showed that 90% of their patients (36 of 40) displayed a significant decrease in left ventricular ejection fraction within 2 h of bypass surgery (50 ± 3% preoperatively to 38 ± 2% postoperatively), with full recovery occurring by 24 h. This occurred despite myocardial protection with multidose hypothermic potassium crystalloid cardioplegia, and was

associated with a significant decrease in cardiac index and left ventricular stroke work index. At 7 days, ejection fraction increased in their patients beyond preoperative levels. Similar studies by Gray et al. (3) showed identical changes in cardiac index and left ventricular stroke work index. Left ventricular ejection fraction in their patients decreased from 58% preoperatively to 41% in the early postoperative period; by day 2, ejection fraction had increased to 61%. Response to volume infusion in the early postoperative period showed flattening and downward displacement of ventricular function curves in 23 of 30 patients, suggesting depression of global left ventricular performance. As in our study, left ventricular filling pressures were maintained in all patients, and the depressed cardiac index and left ventricular ejection fraction appear to represent a decrease in contractility. In their study as well as ours, systemic vascular resistance index did not significantly change in the early postoperative period and excessive afterload could, therefore, not explain the impressive decreases in ejection fraction.

Using gated cardiac blood pool imaging Reduto et al. (4) compared the effects of normothermic intermittent ischemic arrest versus cardioplegia in 57 patients undergoing aortocoronary bypass surgery. Early in the postoperative period, six sequential nuclear studies were performed at 30 min intervals, and significant left ventricular dysfunction (which was normal by 1 week) was seen in 46% of their patients. In their study, left ventricular dysfunction was not observed as often as in some of the other studies, but was found to be independent of the form of myocardial protection used. Mangano (18) noted myocardial dysfunction in all 22 patients evaluated in the early postoperative period. By constructing ventricular function curves and altering preload, left and right ventricular dysfunction occurred early after revascularization but was transient, showing significant recovery within 4 h. As observed by us and others, Mangano (18) also found that recovery of ventricular function was complete in most patients within 24 h of surgery. Thus, it appears that both right and left ventricular dysfunction occur commonly after coronary bypass surgery. This is also supported by the data from the right ventricular ejection fraction catheter used in our study, as well as the radionuclide angiograms that demonstrated the presence of right ventricular dilation and hypokinesia.

Factors associated with postoperative ventricular dysfunction. Not all studies have demonstrated significant myocardial dysfunction after cardiac surgery. The difference may be related to how and when patients were studied, methods of cardioplegia used and therapy in the postoperative setting (19–21). A number of factors could be related to the marked depression in ejection fraction observed after cardiopulmonary bypass surgery. Czer et al. (19) and Fremes et al. (20) suggested that there may be a temperature dependence to the transient changes in ventricular function after bypass surgery. During the period of myocardial rewarming, ejection fraction and myocardial metabolism recovered slowly when cold crystalloid cardioplegia was used. Blood cardioplegia appeared to cause less ischemic injury and was associated with better functional recovery. Myocardial temperatures were consistently warmer with blood cardioplegia, and no consistent temperature dependence was associated with changes in ventricular function. In the present study, core temperatures were improving as myocardial function continued to worsen, suggesting an unlikely role of temperature.

The method of cardioplegia used and the manner in which it is given may play a role in the development of postoperative ventricular dysfunction. Clinical studies comparing blood versus crystaloid cardioplegia have suggested that blood cardioplegia may cause less ischemia injury, but recently this has been brought into question (20–25). Mullen et al. (24) found less perioperative ischemic injury with blood cardioplegia, but postoperatively there were no differences in ventricular performance between blood and crystaloid cardioplegia. Other studies (25) have suggested that the temperature of the blood may be important because, compared with colder solutions, blood cardioplegia >10°C provided decreased myocardial protection. In the present study, blood cardioplegia was chilled to 3°C. Whether cardioplegia is given intermittently or continuously, anterograde or in retrograde manner through the coronary sinus may also have an effect on ventricular function (26,27). Continuous blood cardioplegia has been suggested (26) to be superior to either intermittent blood or crystaloid cardioplegia in metabolically protecting the hypertrophied human heart. Whether other cardioplegic methods would have offered better myocardial protection than that provided by the intermittent blood cardioplegia in this study requires further investigation.

The assessment of ventricular loading conditions, both preload and afterload, may also be important factors to consider. Systemic vascular resistance index did not significantly change from preoperative to immediately postoperative values, but did increase at trough left ventricular function, which could account for some of the depression in left ventricular ejection fraction. This increase in systemic vascular resistance index may be secondary to the depression in left ventricular function and the need to maintain systemic blood pressure. The confounding effect of pressor therapy also needs to be considered. At recovery, systemic vascular resistance index had dramatically improved to 1,808 ± 568 $dyne \cdot s \cdot cm^{-5} \cdot m^2$, as might be expected with known vasodilatory response that occurs hours after operation; it may also be related to the number of the patients receiving intravenous nitroglycerin and nitroprusside. Pulmonary capillary wedge pressure as a measure of preload may also be a significant concern in the postoperative patient. As previously suggested (28,29), pulmonary capillary wedge pressure traditionally used to evaluate left ventricular filling pressure

may not be useful for assessing changes in left ventricular end-diastolic volume in patients after cardiac surgery. Their studies suggest that fluid therapy in such patients could cause a substantial increase in left ventricular end-diastolic volume, with minimal or no change in pulmonary capillary wedge pressure. Other studies (30) indicate that fluid loading after cardiopulmonary bypass can uncover left ventricular dysfunction in the postoperative period. Whether this is secondary to an open pericardium with overdistension of the left ventricle, the use of positive end-expiratory pressure on the ventilator or other factors is unclear. In the present study, postoperative management was designed to maintain a reasonable filling pressure of 10 to 15 mm Hg (pulmonary capillary wedge pressure), but the increases seen in left ventricular end-diastolic volume were not significant enough to explain the degree of ventricular dysfunction.

Other studies (31) have suggested that the magnitude of the early postoperative depression in left ventricular ejection fraction correlated with the preoperative dose of beta-adrenergic blocking agents that patients were receiving. Those patients on higher doses of propranolol had a greater decline in ejection fraction as assessed by a stepwise multiple linear regression analysis. In the present study, preoperative medication had no bearing on the observed results because all patients were taking cardiac medication preoperatively and 66% were taking at least two drugs. Patients receiving a beta-blocker did not demonstrate a greater decline in ventricular function.

Proposed mechanism of ventricular dysfunction. Although the mechanism of ventricular dysfunction in the postoperative period remains unknown, some investigators have suggested that reperfusion injury with oxygen free radicals may play a role. In animal studies, Stewart et al. (32) demonstrated that a cardioplegic solution containing superoxide dismutase, a free radical scavenger, prevented metabolic and functional abnormalities in left ventricular mechanics that were routinely observed in a hypothermic global ischemic and reperfusion canine model. Similar studies (33,34) in a Langendorff-perfused rabbit heart model with 30 min of normothermic global ischemia suggest similar benefits with the use of superoxide dismutase. Other animal studies (35,36) using a regional coronary ischemia-reperfusion model are equally suggestive that oxygen free radicals may cause a depression in ventricular function. The timing of ventricular dysfunction and recovery as seen in the present study is similar to what has been suggested in animal models of reperfusion injury (7,8).

Clinical implications and study limitations. The present study demonstrates that early ventricular dysfunction after coronary bypass surgery continues to be a common problem despite current techniques of myocardial preservation. Serial hemodynamic measurements and the evaluation of ventricular function with the nonimaging nuclear probe and the right ventricular ejection fraction catheter demonstrated that global functional impairment of the right and left ventricles is significant and time dependent in these patients. The use of the nonimaging probe allowed continuous evaluation of ventricular function, which not only predicted hemodynamic deterioration in individual patients, but also indicated when recovery would occur. This type of nonimaging technology may have a role in evaluating patient status and in monitoring early postoperative therapy. This study provides important information as to the time course of these early postoperative events and the role that routine therapy may play. Even though biventricular dysfunction was documented in almost all patients postoperatively in this study, these observations were uncontrolled. In evaluating these patients, many variables are impossible to assess, and differing postoperative management styles may affect the degree to which ventricular dysfunction is observed. The use of inotropic agents, pressors and vasodilators may be common postoperative therapy in some centers, but rarely used in others. Likewise, the role of maintaining ventricular filling pressures (pulmonary capillary wedge pressure >10 mm Hg) could affect the degree of ventricular dysfunction.

In the present study, the use of pressor or inotropic agents appeared to delay the timing of left and right ventricular dysfunction; however, all but one patient had a significant depression in ejection fraction whether or not they were used. One can argue whether ejection fraction should be used to assess myocardial function because it is dependent on both preload and afterload, and study measurements were not made during altered loading conditions. In the present study, however, the overwhelming evidence suggests that the observed decreases in right and left ventricular ejection fraction were due to transient myocardial dysfunction. The right ventricular ejection fraction catheter has its own limitations, but when used for serial measurements, it can demonstrate important trends in the evaluation of right ventricular function.

This present study raises obvious questions about early postoperative morbidity and mortality. Although the initial postoperative course may have been more difficult to manage in some of these patients, no patient had an untoward event. This study group included only patients undergoing routine coronary artery bypass surgery who did not have unstable angina, need for intraaortic balloon pump or prolonged operative time as might occur with a second bypass procedure or concurrent valve replacement. One can only speculate whether groups at higher risk would have greater morbidity and mortality. In the past decade, improvements in operative techniques and myocardial protection have occurred, but transient myocardial dysfunction continues to be a problem in patients undergoing cardiopulmonary bypass. Further studies are needed to evaluate the mechanism of ventricular dysfunction in the early postoperative period and to determine whether it can be prevented. We cannot ascribe the results of this study or others to reperfusion

injury, but there have been some suggestions that a role may exist for free radical scavengers in protecting against this form of postoperative myocardial depression. Future work should be aimed in this direction.

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